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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/517,801

12/10/2004

Stuart James Broughton

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10/04/2006

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EXAMINER

GRAFFEO, MICHEL

ART UNIT

PAPER NUMBER

1614

DATE MAILED: 10/04/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/517,801

Applicant(s)

BROUGHTON ET AL.

Examiner

Michel Graffeo

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1614

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 07 July 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 3-6,9,10,16 and 18 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 3-6,9,10,16 and 18 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

### ***Status of Action***

Claims 3-6, 9-10, 16 and 18 are examined.

Applicant has amended claims 3, 6 and 9, canceled claims 1-2, 7-8 and 17 and provided arguments for the patentability of claims 3-6, 9-10, 16 and 18 in the response filed 7 July 2006.

Applicant's arguments, see response, filed 7 July 2006, have been fully considered and are persuasive to the extent that the rejection under 35 USC §112 and §102, have been withdrawn. Any rejection not specifically stated in this Office Action has been withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

### ***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7 July 2006 has been entered.

***Response to Arguments - 35 USC § 112 1<sup>st</sup> Paragraph***

Applicant's arguments, filed 7 July 2007, have been fully considered and are persuasive for the reasons of record.

***Response to Arguments - 35 USC § 102***

Applicant's arguments, filed 7 July 2007, have been fully considered and are persuasive for the reasons of record.

***Claim Rejections - 35 USC § 103***

Claims 3-6, 9-10, 16 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 93/13055 to The Wellcome Foundation Limited in view of WO/98/30537 to Glaxo Group Limited and US Patent No. 6,297,281 to Chabrier de Lassaunier et al.

WO 93/13055 teaches a pharmaceutical composition and methods (see page 1 lines 5-6) comprising (2S)-2-amino-4-[[2-(ethanimidoylamino)ethyl]thio] butanoic acid and a phosphoric acid thereof (claim 2 – see page 8 line 8) wherein R<sup>1</sup> is CH<sub>3</sub>, Q is CH<sub>2</sub>CH<sub>2</sub>XCH<sub>2</sub>CH<sub>2</sub> and X is S of the compound below (see Abstract):



a bulking agent, such as tragacanth (see page 10 line 12), which itself contains small amounts of cellulose and starch (claim 8), and an antioxidant (see page 9 line 30) for the treatment in a human (claims 9 and 16) of a condition where there is an

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advantage of inhibiting NO production from L-arginine by the action of NO synthase (see page 4 lines 15-20) such as arthritis (claim 10 – see page 5 lines 20-24).

WO 93/13055 does not specifically teach solvates of (2S)-2-amino-4-[[2-(ethanimidoylamino)ethyl]thio] butanoic acid or any particular chelating agents and amounts thereof or amounts of bulking agents present in the pharmaceutical composition. Nonetheless, given the references below which describe chelating agents, one of ordinary skill in the art would through routine optimization appreciate the composition comprising 0.1 to 5% of the active agent, 80-99.5% of the bulking agent and 0.005 to 5% of the antioxidant particularly since bulking agents for example are used in higher amounts as a filler (claim 6). In other words, it would be obvious to one skilled in the art to use each additive in an amount appropriate for that additive.

The WO/98/30537 reference teaches the NO synthase inhibitor (2S)-2-amino-4-[[2-(ethanimidoylamino)ethyl]thio] butanoic acid and salts and solvates thereof (claims 2-5 – see page 2 line 26). Although the reference does not recite the particular solvates, mono and trihydrates, absent evidence to the contrary, one of ordinary skill in the art would appreciate the presence of such hydrates from the mention of solvates in the reference.

Chabrier de Lassaunier et al. teach a pharmaceutical composition containing at least one NO synthase inhibiting substance and at least one oxygen reactive form trapping substance (see Abstract) such as those substances with antioxidant properties (see col 2 lines 42-45) and in particular ascorbic acid (claim 7-see col 4 line 40).

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One of ordinary skill in the art would have been motivated to combine the above references and as combined would make obvious the invention as claimed. One of ordinary skill in the art would have been motivated to combine WO 98/30537 with WO 93/13055 because WO 98/30537 cites WO 93/13055. One of ordinary skill in the art would have been motivated to combine Chabrier de Lassaunier et al. with WO 98/30537 and WO 93/13055 because Chabrier de Lassaunier et al. teach the combination of at least one NO synthase inhibitor combined with another agent having antioxidant properties and both WO 98/30537 and WO 93/13055 teach NO synthase inhibitors and WO 93/13055 teaches the combination of a NO synthase inhibitor combined with an antioxidant as well. Thus, the claimed invention was within the ordinary skill in the art to make and use at the time it was made and was as a whole, *prima facie* obvious.

### ***Response to Arguments - 35 USC § 103***

Applicant's arguments filed 8 December 2005 have been fully considered but they are not persuasive.

Applicant continues to maintain that the claimed active agent is not found in the '055 reference. This is not persuasive since the reference discloses (and claims, see claim 6 for example) the active claimed in the instant Application. Moreover, Applicant has not pointed out how the '055 reference is lacking in its disclosure of the claimed active agent. Additionally, the '055 reference obviates the inclusion of antioxidants in the formulation even when such is a solid formulation. See particularly the first paragraph on page 9 which includes liquid solutions of the active agent in oral capsules

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and tablets. Thus, the combined references teach and make prima facie obvious how to use the claimed invention at the time that it was made.

### ***State of the Art***

US Patent No. 5,889,056 to Hodson et al. and 6369272 to Beams et al. are considered substantial equivalents to WO 93/13055 to The Wellcome Foundation Limited.

### ***Conclusion***

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michel Graffeo whose telephone number is 571-272-8505. The examiner can normally be reached 9am to 5:30pm Monday to Friday.


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

25 September 2006

MG

 9/28/06  
ARDIN H. MARSCHEL  
SUPERVISORY PATENT EXAMINER